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Evaluating the Long-Term Health Impact of Military Service

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Does military service, in particular operational deployment, result in a higher risk of chronic illness among military personnel and veterans? The Millennium Cohort Study, the largest Department of Defense prospective study ever conducted, will attempt to answer this question.(1)

Legacy of the Gulf War

The 1999 Institute of Medicine report, *Measuring Health*,⁽²⁾ recommended the Department of Defense (DOD) begin systematically collecting population-based data to evaluate the health of service personnel throughout their military careers and after separation from military service. DOD, in its report to Congress titled *Effectiveness of Medical Research Initiatives Regarding Gulf War Illnesses*,⁽³⁾ also identified the need for a coordinated effort to determine whether deployment-related exposures are associated with post-deployment health outcomes. The Millennium Cohort Study was developed in response to these recommendations.

Soon after fighting ended in Operation Desert Storm, numerous Gulf War veterans began reporting various medical symptoms. Many of these veterans attributed their illnesses to deployment-related expo-

sures in the Gulf War. At that time, DOD had little systematically collected pre-deployment health data to compare with post-deployment health assessments. In addition, all analyses of Gulf War veterans were retrospective in design. Epidemiologically, a prospective, or forward-looking design is considered much stronger. The Millennium Cohort Study takes an important step in support of force health protection by providing longitudinal health data, previously lacking, on a large cohort of military service personnel over a 21-year period. These essential data will assist researchers and military leaders in understanding the health impact of military deployments more completely than in the past. In turn, this better understanding may affect deployment policies as well as prevention and treatment programs.

Development of the Project

A multi-service and multi-agency team was assembled to create a comprehensive study encompassing all branches of military service, including Reserve and National Guard personnel. The first task accomplished by this collaborative team was articulating the objectives of the study. The primary objective is to determine if risk factors related to military service, such as service occupational specialty, deployment history, service type, and other exposures, are associated with the development of chronic disease. Secondary objectives include examining characteristics of military service associated with common clinician-diagnosed diseases and with functional status, as measured by scores on several standardized self-reported health inventories. To meet these



objectives, a survey was created that will be distributed every 3 years for the next 21 years.

The initial survey instrument includes information on basic demographics; the 36-item Short Form for Veterans of the Medical Outcomes Survey (SF-36V)(4) physical and functional status score; the Patient Health Questionnaire (PHQ)(5) to provide a psychosocial assessment; medical conditions diagnosed by a clinician; self-reported symptoms; the Patient Checklist (PCL-17)(6) to screen for post-traumatic stress disorder; alcohol use;(7) tobacco use; alternative medicine use; occupational classification; life events and occupational exposures; sleep and nutrition; and various contact information questions. In addition, the survey instrument affords respondents an opportunity to list any concerns not otherwise solicited. The standardized instruments (SF-36V, PHQ, and PCL-17) were selected because of published data on their reliability and validity, and their use in previous veterans' studies.(8)

Because surveying all military personnel is not feasible, a study population was generated as a statistical sample of all regular active duty, National Guard, and Reserve military personnel of the Army, Navy, Air Force, and Marine Corps, so as to be representative of the entire military force. The initially enrolled cohort is stratified to include 30,000 study participants who have been deployed to Southwest Asia, Bosnia, and Kosovo, and 70,000 study participants who have never been deployed to these areas. Reserve, National Guard, and female service personnel will be over-sampled (see Fig. 1) so that adequate numbers of these groups will be available for meaningful statistical analyses. Service

members' data were provided by the Defense Manpower Data Center, Monterey Bay, CA. This strategy should generate a probability-based sample of 100,000 study participants who were in service as of 1 October 2000, representing approximately 3.7 percent of the 2.7 million persons in uniform. Figure 1 reflects the expected number of potential participants that must be targeted to enroll the initial 100,000 individuals. In 2004, and again in 2007, additional probability-based samples of 20,000 U.S. active duty, National Guard, and Reserve military personnel will be added to the study (see Fig. 2). These personnel will have at least 1 year and not more than 2 years of service at the time of recruitment into the study, and will provide representation of newer military members who were not represented at initial enrollment.

Methodology

The Millennium Cohort Study questionnaire is distributed using standard postal survey techniques.(9,10) These techniques consist of sending introductory and reminder postcards, alternating with postal surveys, for several iterations. A tracking service and several address locator databases are used to find correct addresses for undelivered mail. This process will be repeated with participants every 3 years. Email messages may also be sent to encourage participation.

In conjunction with the mailed survey, the Millennium Cohort Study research staff also created an Internet site. The website (www.MillenniumCohort.org) serves as an inexpensive means to receive data, as well as an efficient system to disseminate information to study participants and the general public. The website provides participants

with the option to complete an online questionnaire in place of the mailed paper version. The use of a "digital signature"(11,12) (the subject identification number along with the last four digits of the social security number) prevents individuals other than study subjects from completing the survey. The format of the online questionnaire is identical to the paper version, but it is less time-consuming to complete. After the participant completes and submits the questionnaire, the data are transmitted via very secure electronic means to the Naval Health Research Center, San Diego, CA, and incorporated into the study database.

An added benefit of the website is that it provides a nearly instantaneous method of communication between subjects and investigators. Subjects may provide mailing address changes and/or their email addresses to receive periodic study communications. Additionally, the website text can be easily modified to provide up-to-the-minute study progress reports and findings to participants. Participants are able to easily contact the study coordinator via email to ask questions or offer suggestions. Thus, the website serves as a continuous and relatively inexpensive means for keeping study participants involved and interested throughout the course of the study. Recognizing the cost and speed advantages of online participation, the Millennium Cohort Study research staff is working hard to maximize participation through this route.

After candidates have consented to participate and respond to the survey, 1 percent of them will be asked to complete a similar but shorter survey instrument to assess the reliability of selected questions. Additionally, self-reported hospital-

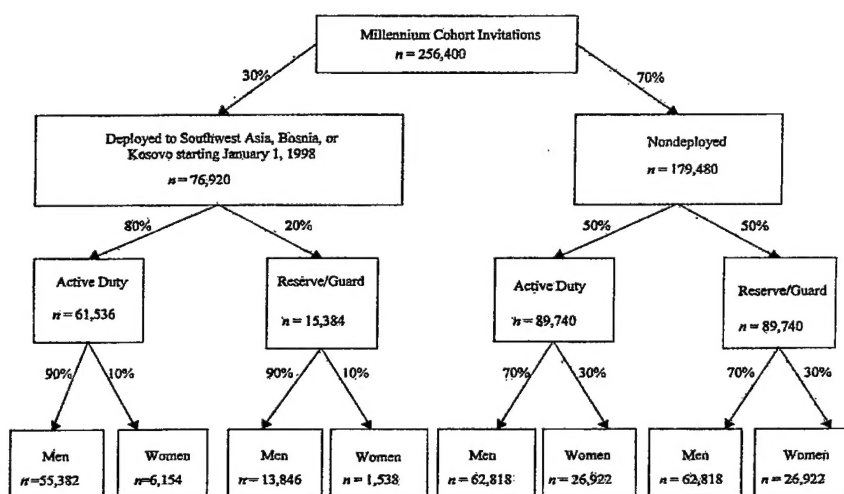


Figure 1: Sampling Strategy.
An initial sample of 256,400 service men and women was drawn from regular active duty, Reserve and National Guard rosters as of 1 October 2000, in an attempt to achieve the 100,000 target population size. Thirty percent of this population was deployed to Southwest Asia, Bosnia, or Kosovo after 1 January 1998, and 70 percent were not deployed to these areas. Women and Reserve/National Guard personnel were over-sampled.

ization data will be validated by linkage to the Department of Defense's electronic hospitalization databases. Similarly, various Department of Veterans Affairs databases will be examined for healthcare utilization. These electronic records archive clinical diagnoses in the International Classification of Diseases, 9th Revision, Clinical Modification format.(13)

The DOD Center for Deployment Health Research directly manages or has access to numerous established military data sets.(14-17) These data sources will be linked to survey data and enhance the ability to conduct comprehensive evaluations of the medical outcomes of interest. In addition, the Department of Veterans Affairs has agreed to provide mortality and other healthcare utilization and disability compensation data that will augment the investigators' capacity to capture health outcomes in longitudinal follow-up.(18-20) Self-reported and objective electronic data will be examined for health outcomes of interest by demographic and deployment subgroups. Demographic covariates available for multivariable

modeling will include age, gender, race/ethnicity, marital status, education level, rank/rate, occupation, service branch, and length of service. In addition, health habits, healthcare utilization history, immunization history, and deployment history will be available from the survey and other sources to uniquely describe exposures of military concern. Outcomes of interest are expected to be extensive, and will include common chronic diseases, such as diabetes, heart disease, and cancer. Other outcomes that may be uniquely accessible from the periodic surveys include chronic, multi-symptom illnesses and more subtle changes in functional status. Interest in these diagnostically challenging outcomes continues to grow more than a decade after the Persian Gulf War experience.(2,3)

A major challenge in conducting cohort studies is maximizing participation, both initial enrollment of study subjects and prevention of losses to follow-up.(21) To promote a sense of unity among study participants and encourage a higher response rate, study investigators developed a

Millennium Cohort Study logo that appears on all correspondence, questionnaires, and incentives. Millennium Cohort Study staff members have actively sought the support of military and veterans service organizations to further instill a sense of unity and duty. In August 2000, a special study briefing was given to Washington, DC, area military and Veterans Service Organization representatives. A number of these organizations have subsequently agreed to endorse and help publicize the study, and each of these endorsements appears on the website. Most recently, the Deputy Secretary of Defense, Paul Wolfowitz, provided a letter of endorsement to the Millennium Cohort Study, that was mailed to subjects and placed on the website. Other methods of maintaining contact with participants and keeping them involved in the study are continuously explored.

Why Create a "Cohort"?

The longitudinal cohort study design method is a natural choice for a study of this importance and magnitude. The cohort study offers

several advantages over other study designs. In particular, cohort studies are valuable when the exposure or exposures being examined are rare.⁽²²⁾ This advantage is especially relevant to the unique roles and duties presented by the military population. Cohort studies also allow for the examination of "multiple effects of a single exposure." The ability to examine the relationship between exposure and the time before disease presents itself is an important strength of the cohort study as well. Prospective cohort studies reduce the chance of participant recall bias inherent in most retrospective study designs. Further, cohort studies that examine data sources such as medical and deployment records supplemented with participant questionnaires, like the Millennium Cohort Study, provide a more complete method of collecting information on exposures. The cohort design method allows investigators to periodically resurvey the study population, providing flexibility in assessments based on newly discovered scientific advancements.⁽²²⁾ As noted previously, the Millennium Cohort Study takes advantage of these design features by surveying the selected cohort every 3 years, for a total of seven questionnaires within the 21-year study period.

The nature of the cohort study, providing the most direct measurement of the risk of disease development by prospectively collecting and studying exposure and outcome data over time, has been responsible for numerous public health advancements. The Millennium Cohort Study has the potential to contribute new and important information to the field of preventive medicine and public health, benefiting both military and civilian populations alike just as other landmark cohort

studies have done. Two seminal longitudinal prospective cohort studies, the Framingham Heart Study⁽²⁴⁾ and the Nurses' Cohort Study,⁽²³⁾ have been able to provide valuable insight with regard to the identification of risk factors for diseases of public health importance. The Framingham Heart Study, through its tracking of a cohort of 5,127 men and women living in a single community, identified risk factors for cardiovascular disease that greatly enhanced our scientific understanding of the association between lifestyle factors and the occurrence of adverse outcomes due to coronary artery disease. The Nurses' Cohort Study was initiated to examine the health effects of the use of contraception among women. By leveraging the cohort design, this study has since provided invaluable information on reproductive system cancers and other women's health issues. In a similar manner, the Millennium Cohort Study has the potential to uncover unanticipated exposure-disease associations in a relatively young, healthy, screened population that might otherwise remain unrecognized. It is likely that this information will not only benefit the military, but the civilian populations as well, just as the Framingham and Nurses' Cohort studies benefited more than just their respective study populations. Most members of the Millennium Cohort Study population will become civilians during the course of follow-up, further highlighting the applicability of study findings in both military and civilian sectors.

Conclusion

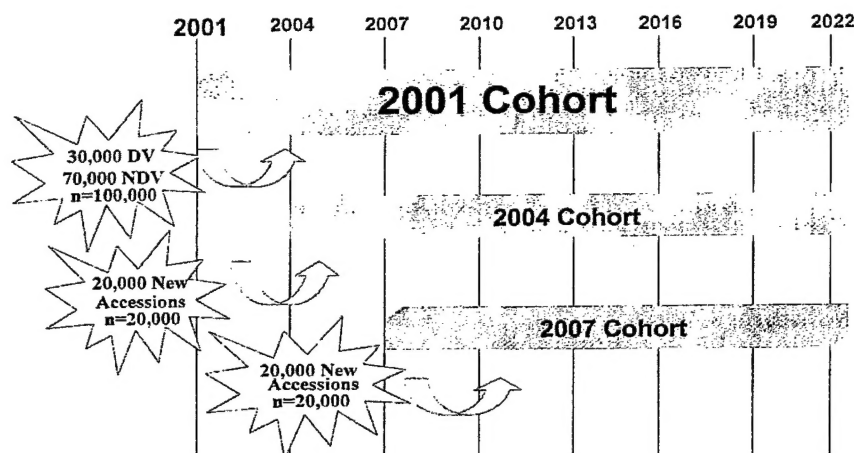
Millennium Cohort Study data will likely serve as a foundation for other epidemiological studies, just as other landmark cohort studies have done before. While military research teams

will manage many of these efforts, civilian research teams will likely be interested in the Millennium Cohort Study results as well. Because of its potential impact on preventive medicine practice, the Millennium Cohort Study is an important and exciting project for the new millennium. The study's successful implementation is critical, and its results may resonate in public health for years to come.

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Figure 2: The Millennium Cohort Study Timeline



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